

**Version with Markings to Show Changes Made**

1st complete paragraph, page 71, lines 11-14:

“As an example of redundant substring template generation, consider the following short amino acid sequence retained as a string vector of amino acid one letter representations:

AIRCKSMLRYGHAMQLREWVCCMHAMQVYRLM (SEQ ID NO:94)”

2nd complete paragraph, page 71, line 15 to page 72, line 3:

“If we chose to apply the template-generating algorithm directly to this series, the search algorithm would begin by looking for two copies of the first half of the series, AIRCKSMLRYGHAMQL (SEQ ID NO:95). Next it would assess the starting positions and frequency of occurrence of the substring from which the last amino acid, L has been dropped, i.e., AIRCKSMLRYGHAMQ (SEQ ID NO: 96), and so on, looking at each possible substring in the first half of the sequence. The algorithm finds one redundant substring, HAMQ, occurring twice starting at positions 12 and 24. A generalization of this method also allows for the search of substrings that are both “backward” and “forward” in orientation in the original sequence. Such a search of our example string also turns up the twice repeated substring MLRY, appearing at starting position 7 in a “forward” orientation and at starting position 29 in a “backward” orientation. Our  $R_{temp}$  might then equal one or both of these specific amino acid substrings in some order and orientation.”

2nd complete paragraph, page 80, line 18 to page 81, line 17:

“Figures 4A-4D summarize the EAR responses to dopamine infusion with respect to the influence of SHQR (SEQ ID NO:1) and THQA (SEQ ID NO:2) in the two

D<sub>2</sub>DA receptor-transfected cell systems, in which the former significantly potentiated the dopamine-induced increment in total milli-pH units in both cell systems. We report the results of one-tailed t-tests with pairing within chamber as  $t_{(\#)}$ , where # represents the degrees of freedom of the paired comparison and  $\rho$  denotes the probability of such results occurring by chance. For the SHQR peptide (SEQ ID NO:1) in the LtK system,  $t_{(3)} = 13.28$ ,  $\rho = 0.0009$ , and for the SHQR peptide (SEQ ID NO:1) in the CHO cell system,  $t_{(3)} = 28.06$ ,  $\rho < 0.0001$ . THQA (SEQ ID NO:2) did not significantly potentiate the dopamine response in either system,  $t_{(3)} = 0.620$  and  $t_{(3)} = 1.309$ ,  $\rho > 0.05$ , respectively. Figures 5A-5D contain graphs of the influence of the peptides E...PL (SEQ ID NO:3) and E...PY (SEQ ID NO:4) on the EAR response to dopamine in the two D<sub>2</sub>DA receptor-transfected cell systems. Both peptides demonstrated statistically significant activation,  $t_{(7)} = 25.47$ ,  $\rho < 0.0001$  and  $t_{(3)} = 69.830$ ,  $\rho < 0.0001$ , respectively, in the LtK system. However, neither of the E...PL (SEQ ID NO:3) and E...PY (SEQ ID NO:4) peptides influenced the dopamine-induced EAR of the CHO cells significantly, with  $t_{(3)} = 1.542$ ,  $\rho > 0.05$  and  $t_{(7)} = 1.283$ ,  $\rho > 0.05$ , respectively. Three of the remaining eight peptides exhibited statistically significant effects on at least one of the two receptor-transfected cell systems (Table 3). The overall "hit rate", as measured by modulation of the kinetics of the EAR of two transfected cell lines to dopamine, for these peptides was thus 50% (i.e., six of twelve peptide candidates that were synthesized and tested statistically significantly altered EAR in one or both of the D<sub>2</sub>DA receptor-transfected cell systems used). All D<sub>2</sub>DA targeted peptides whose effects reached significance increased EAR."

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1st complete paragraph, page 81, lines 18-22:

“A set of EAR dose response curves were computed for the SHQR peptide (SEQ ID NO:1) across concentrations of dopamine ( $10^{-8.5}$  M to  $10^{-5.5}$  M) and the SQHR peptide (SEQ ID NO:1; [(])10 nM to 3  $\mu$ M) (not shown). LtK cells were used for these experiments. The resulting dose response curves manifested asymptotic sigmoidal kinetics, suggestive of positive cooperativity.

Table 7, page 88:

Examples of Human Calcitonin-Targeted Peptides from Non-Overlapping Redundant Substring Template of Human Calcitonin					
<u>SEQ ID</u>	<u>Sequence</u>	<u>SEQ ID</u>	<u>Sequence</u>	<u>SEQ ID</u>	<u>Sequence</u>
<u>34</u>	KPNLPNELNK	<u>54</u>	VGTLNPAFSV	<u>74</u>	MNSIQTDFTM
<u>35</u>	VTNLGNHIGV	<u>55</u>	CGNYGTRFSK	<u>75</u>	VQSLTNDISK
<u>36</u>	CNNFSPDITV	<u>56</u>	CSSLQQALTV	<u>76</u>	KGNINPAYNV
<u>37</u>	MQQITTHFQC	<u>57</u>	MPSIPTHLNK	<u>77</u>	KTGLNNEINV
<u>38</u>	VNTFGTELSC	<u>58</u>	KNNYGQAFTV	<u>78</u>	VQSFTNEIQC
<u>39</u>	CNNIGNRLSC	<u>59</u>	KNQLNTEINC	<u>79</u>	KTTINGHISK
<u>40</u>	KGNFTPEWPC	<u>60</u>	KNPLNNHLNM	<u>80</u>	VGGYGTDYNM
<u>41</u>	MGPLPQAFQC	<u>61</u>	VNGIGQAINV	<u>81</u>	MQGYTNDIPV
<u>42</u>	KSNIGPALTM	<u>62</u>	CPGITGDFQK	<u>82</u>	VNQWQNHYTM
<u>43</u>	VSQYGQELQV	<u>63</u>	MTQFQSHITV	<u>83</u>	KPTFSNAYNV
<u>44</u>	VSPYQSHFNV	<u>64</u>	VQTYPPHFPV	<u>84</u>	VTNFSNALSM
<u>45</u>	MGGWGPALNC	<u>65</u>	KGNLNTDLNM	<u>85</u>	VTPINSEFPC
<u>46</u>	CTGYTNAIQM	<u>66</u>	VTPLSSAINK	<u>86</u>	KNQLNTHIGK
<u>47</u>	MNTLQQAYPK	<u>67</u>	VNNLSSEYNV	<u>87</u>	VQSINNAIGK
<u>48</u>	VQPYNGELNM	<u>68</u>	MPPWPSDYPC	<u>88</u>	MGTFFQPDWQV
<u>49</u>	VTNWNGRINK	<u>69</u>	KQSFQSELNK	<u>89</u>	VQTISSRWGK
<u>50</u>	MQNFPTAINV	<u>70</u>	VPSLTTRLQV	<u>90</u>	MGNITQDLQC
<u>51</u>	VPSIQGHYGM	<u>71</u>	VQPLQGHLPV	<u>91</u>	KGSYTTELGV
<u>52</u>	VGNLTQHYTK	<u>72</u>	VSQFNQAWGV	<u>92</u>	KNSYSPELTV
<u>53</u>	VPPFTNHWQK	<u>73</u>	VPSLNSALGV	<u>93</u>	CNSYTPEFPC

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**Remarks**

No new matter is being added by these amendments. Corrections in the specification add SEQ ID NO's where appropriate. In addition, a sequence listing is being submitted to reflect the omission of the sequence listing in the original filing. The Applicants respectfully request that the above amendments be entered into the application.

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Respectfully submitted,



Mary S. Consalvi  
Reg. No. 32,212

HOWREY SIMON ARNOLD & WHITE, LLP  
Box No. 34  
301 Ravenswood Avenue  
Menlo Park, CA  
Direct Dial: (650) 463-8400

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